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FLICE, a novel FADD-homologous ICE/CED-3-like protease, is recruited to the CD95 (Fas/APO-1) death--inducing signaling complex.

Muzio M, Chinnaiyan AM, Kischkel FC, O'Rourke K, Shevchenko A, Ni J, Scaffidi C, Bretz JD, Zhang M, Gentz R, Mann M, Krammer PH, Peter ME, Dixit VM.

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To identify CAP3 and CAP4, components of the CD95 (Fas/APO-1) death-inducing signaling complex, we utilized nano-electrospray tandem mass spectrometry, a recently developed technique to sequence femtomole quantities of polyacrylamide gel-separated proteins. Interestingly, CAP4 encodes a novel 55 kDa protein, designated FLICE, which has homology to both FADD and the ICE/CED-3 family of cysteine proteases. FLICE binds to the death effector domain of FADD and upon overexpression induces apoptosis that is blocked by the ICE family inhibitors, CrmA and z-VAD-fmk. CAP3 was identified as the FLICE prodomain which likely remains bound to the receptor after proteolytic activation. Taken together, this is unique biochemical evidence to link a death receptor physically to the proapoptotic proteases of the ICE/CED-3 family.

PMID: 8681377 [PubMed - indexed for MEDLINE]

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